



Clinical trial results:

A Multicenter, Open-Label, Long-Term Extension Of Phase III Studies (BN29552/BN29553) Of Crenezumab In Patients With Alzheimer's Disease

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2017-002702-12 |
| Trial protocol | ES DE LT GB SE DK FI HU FR BE PL IT |
| Global end of trial date | 31 May 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v2 (current) |
| This version publication date | 29 July 2020 |
| First version publication date | 11 June 2020 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | BN40031 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03491150 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 31 May 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 31 May 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety of Crenezumab

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 11 April 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Australia: 3 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | Finland: 3 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Hong Kong: 1 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Lithuania: 1 |
| Country: Number of subjects enrolled | Mexico: 6 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | Russian Federation: 6 |
| Country: Number of subjects enrolled | Turkey: 1 |
| Country: Number of subjects enrolled | United States: 85 |
| Worldwide total number of subjects | 149 |
| EEA total number of subjects | 30 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 23 |
| From 65 to 84 years | 118 |
| 85 years and over | 8 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 66 centers in 16 countries.

Pre-assignment

Screening details:

A total of 149 subjects were enrolled at 66 centers. These 149 subjects represented the Safety Analysis population and data for this population is presented here.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Parent Placebo |

Arm description:

Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

| | |
|--|---------------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Crenezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Crenezumab was administered by Intravenous (IV) infusion every 4 weeks (Q4W) at a dose of 60mg/kg.

| | |
|------------------|-------------------|
| Arm title | Parent Crenezumab |
|------------------|-------------------|

Arm description:

Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Crenezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Crenezumab was administered by Intravenous (IV) infusion every 4 weeks (Q4W) at a dose of 60mg/kg.

| Number of subjects in period 1 | Parent Placebo | Parent Crenezumab |
|---------------------------------------|----------------|-------------------|
| Started | 76 | 73 |
| Completed | 0 | 0 |
| Not completed | 76 | 73 |
| Consent withdrawn by subject | 1 | 2 |
| Adverse event, non-fatal | 1 | - |
| Unknown | - | 1 |
| Study Terminated by Sponsor | 74 | 70 |

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Parent Placebo |
| Reporting group description: | |
| Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W). | |
| Reporting group title | Parent Crenezumab |
| Reporting group description: | |
| Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W). | |

| Reporting group values | Parent Placebo | Parent Crenezumab | Total |
|--|----------------|-------------------|-------|
| Number of subjects | 76 | 73 | 149 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 10 | 13 | 23 |
| From 65-84 years | 59 | 59 | 118 |
| 85 years and over | 7 | 1 | 8 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 73.8 | 72.0 | |
| standard deviation | ± 7.6 | ± 7.6 | - |
| Sex: Female, Male | | | |
| Units: | | | |
| Female | 37 | 38 | 75 |
| Male | 39 | 35 | 74 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 6 | 3 | 9 |
| Not Hispanic or Latino | 69 | 69 | 138 |
| Not Stated | 1 | 1 | 2 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Asian | 4 | 2 | 6 |
| Black or African American | 0 | 1 | 1 |
| Unknown | 0 | 3 | 3 |
| White | 72 | 67 | 139 |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | Parent Placebo |
| Reporting group description: | |
| Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W). | |
| Reporting group title | Parent Crenezumab |
| Reporting group description: | |
| Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W). | |

Primary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[1] |
|-----------------|---|

End point description:

An Adverse Event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline up to 16 weeks after the last dose of study drug (up to 54 weeks).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed as this study has only one arm.

| End point values | Parent Placebo | Parent Crenezumab | | |
|-------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76 | 73 | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| AEs | 32.9 | 42.5 | | |
| SAEs | 3.9 | 5.5 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-Crenezumab Antibodies

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Anti-Crenezumab Antibodies ^[2] |
|-----------------|---|

End point description:

Please note that for this Outcome Measure, no Subjects were evaluated at all as the existing immunogenicity data from a parent study (Study BN29552) showed a low potential of Crenezumab to induce Anti-Drug Antibodies (ADAs).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline up to end of study (up to 54 weeks).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed as this study has only one arm.

| End point values | Parent Placebo | Parent Crenezumab | | |
|-------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[3] | 0 ^[4] | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |

Notes:

[3] - ADAs were not collected in this study due to low induction potential of Crenezumab.

[4] - ADAs were not collected in this study due to low induction potential of Crenezumab.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 16 weeks after the last dose of study drug (up to 54 weeks).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Parent Placebo |
|-----------------------|----------------|

Reporting group description:

Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

| | |
|-----------------------|-------------------|
| Reporting group title | Parent Crenezumab |
|-----------------------|-------------------|

Reporting group description:

Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

| Serious adverse events | Parent Placebo | Parent Crenezumab | |
|---|----------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 76 (3.95%) | 4 / 73 (5.48%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| FALL | | | |
| subjects affected / exposed | 0 / 76 (0.00%) | 1 / 73 (1.37%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 76 (1.32%) | 0 / 73 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| OPTIC ISCHAEMIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 76 (0.00%) | 1 / 73 (1.37%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|-----------------------------|---|----------------|----------------|--|
| Gastrointestinal disorders | INCARCERATED INGUINAL HERNIA | | | |
| | subjects affected / exposed | 1 / 76 (1.32%) | 0 / 73 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| | RECTAL HAEMORRHAGE | | | |
| | subjects affected / exposed | 1 / 76 (1.32%) | 0 / 73 (0.00%) | |
| Infections and infestations | occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| | PNEUMONIA | | | |
| | subjects affected / exposed | 0 / 76 (0.00%) | 1 / 73 (1.37%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UROSEPSIS | subjects affected / exposed | 0 / 76 (0.00%) | 1 / 73 (1.37%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| | | | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Parent Placebo | Parent Crenezumab | |
|---|----------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 76 (5.26%) | 4 / 73 (5.48%) | |
| Injury, poisoning and procedural complications | | | |
| FALL | | | |
| subjects affected / exposed | 4 / 76 (5.26%) | 4 / 73 (5.48%) | |
| occurrences (all) | 5 | 4 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 05 August 2018 | Following updates were made: [1] Improved alignment with CREAD 1 and 2 parent studies; [2] Language updated for China as China extensions activated in CREAD 1/2 studies; [3] Updating of information to align with latest Investigator's brochure; [4] Updates made to Exploratory Efficacy Objectives; [5] Number of Sites amended; [6] Recruitment period updated based on shortening of recruitment periods for CREAD 1/2 studies; [7] First Dose Window duration amended; [8] Update to Inclusion Criteria; [9] Addition of text to recognize country variability in designation of non-investigational medicinal product/investigational medicinal product status to positron emission tomography (PET) tracers; [10] Modification of physical and neurologic examination assessment; [11] Harmonisation of Vital Signs language and [12] Further updates including to Lab Samples, PD Biomarkers, Safety, Patient withdrawal, order of Clinical Assessments, timing of Brain MRI and Schedule of Activities. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was discontinued due to an interim analysis in the BN29552 study, which indicated that Crenezumab was unlikely to meet its primary endpoint.

Notes: